

Spinal ischemic paraplegia: modulation by human embryonic stem cell implant.

## Grant Award Details

Spinal ischemic paraplegia: modulation by human embryonic stem cell implant.

**Grant Type:** Comprehensive Grant

**Grant Number:** RC1-00131

**Investigator:**

**Name:** Martin Marsala

**Institution:** University of California, San Diego

**Type:** PI

**Disease Focus:** Neurological Disorders, Spinal Cord Injury

**Human Stem Cell Use:** Embryonic Stem Cell

**Award Value:** \$2,356,090

**Status:** Closed

## Progress Reports

**Reporting Period:** Year 2

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**Reporting Period:** Year 3

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**Reporting Period:** Year 4

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## Grant Application Details

**Application Title:** Spinal ischemic paraplegia: modulation by human embryonic stem cell implant

**Public Abstract:**

schemia-induced paraplegia often combined with a qualitatively defined increase in muscle tone (i.e. spasticity and rigidity) is a serious complication associated with a temporary aortic cross-clamping ( a surgical procedure to repair an aortic aneurysm). In addition to spinal ischemic injury-induced spasticity and rigidity a significant population of patients with traumatic spinal injury develop a comparable qualitative deficit i.e. debilitating muscle spasticity. At present there are no effective treatment which would lead to a permanent amelioration of spasticity and rigidity and corresponding improvement in ambulatory function. In recent studies, by using rat model of spinal ischemic injury we have demonstrated that spinal transplantation of rat or human neurons leads to a clinically relevant improvement in motor function and correlates with a long term survival and maturation of grafted cells. More recently we have demonstrated a comparable maturation of human spinal precursors grafted spinally in immunosuppressed minipig. In the proposed set of experiments we wish to characterize a therapeutical potential of human blastocyst-derived neuronal precursors when grafted into previously ischemia- injured rat or minipig spinal cord. Defining the potency of spinally grafted hESC-derived neuronal precursors in two in vivo models of spinal ischemic injury serves to delineate the differences and/or uniformity in the cell maturation when cells are transplanted in 2 different animals species and can provide an important data set for future implications of such a therapies in human patients.

**Statement of Benefit to California:**

Traumatic or ischemic spinal cord injury affect a significant number of people and in majority of cases can lead to a variable degree of motor dysfunction (such as paraparesis or paraplegia) and often combined with increased muscle tone (i.e. spasticity and rigidity). In contrast to other organ systems the central nervous system and spinal cord in particular has minimal or no neuron-regenerative capacity and therefore if a significant population of spinal cord neurons or fibers is lost the resulting deficit is permanent and irreversible. At present there is no effective therapy which would lead to a clinically relevant neurological improvement in patients with ischemia or trauma-induced paraplegia. Initial experimental data using paraplegic rats show that spinal grafting of rat or human neuronal precursors can provide a significant amelioration of spasticity and lead to improved ambulatory function. In the proposed set of experiments we wish to characterize a therapeutical potential of human blastocyst-derived neuronal precursors when grafted into previously ischemia- injured rat or minipig spinal cord. If proven effective such a treatment can potentially be used in patients with spinal ischemic paraplegia or in patients with other spinal injury-related dysfunction associated with a region-specific neuronal loss.

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